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FILE 'HOME' ENTERED AT 10:24:52 ON 01 JUN 2009

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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DICTIONARY FILE UPDATES:  31 MAY 2009  HIGHEST RN 1151391-70-6

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=> E "VITAMIN D3"/CN 25
E1            1     VITAMIN D2-6-T/CN
E2            1     VITAMIN D2-TETRACYANOETHYLENE ADDUCT/CN
E3            1 --> VITAMIN D3/CN
E4            1     VITAMIN D3 25-HYDROXYLASE/CN
E5            1     VITAMIN D3 25-HYDROXYLASE (HUMAN CELL LINE HEPG2 GENE CYP 27)/CN
E6            1     VITAMIN D3 25-HYDROXYLASE (P 450 27A)/CN
E7            1     VITAMIN D3 25-HYDROXYLASE (RAT CLONE PLMT25)/CN
E8            1     VITAMIN D3 3-AMINOPROPYL ETHER/CN
E9            1     VITAMIN D3 3B-SULFATE/CN
E10           1     VITAMIN D3 ACETATE/CN
E11           1     VITAMIN D3 ALLOPHANATE/CN
E12           1     VITAMIN D3 BENZOATE/CN
E13           1     VITAMIN D3 CAPROATE/CN
E14           1     VITAMIN D3 GLUCOSIDE/CN
E15           1     VITAMIN D3 HEMISUCCINATE/CN
E16           1     VITAMIN D3 ISOBUTYRATE/CN
E17           1     VITAMIN D3 ISOVALERATE/CN
E18           1     VITAMIN D3 LAURATE/CN
E19           1     VITAMIN D3 MYRISTATE/CN
E20           1     VITAMIN D3 N-ACETYLGLUCOSAMINIDE/CN
E21           1     VITAMIN D3 P-NITROBENZOATE/CN
E22           1     VITAMIN D3 PALMITATE/CN
E23           1     VITAMIN D3 PHENYLACETATE/CN
E24           1     VITAMIN D3 PHOSPHODICHLORIDATE/CN
E25           1     VITAMIN D3 PROPIONATE/CN

=> S E3
L1            1 "VITAMIN D3"/CN
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=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       5.83       6.27

FILE 'CAPLUS' ENTERED AT 10:26:50 ON 01 JUN 2009
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FILE COVERS 1907 - 1 Jun 2009  VOL 150 ISS 23
FILE LAST UPDATED: 31 May 2009  (20090531/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Feb 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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=> s l1/thu
          7098 L1
       1129867 THU/RL
L2        1256 L1/THU
                (L1 (L) THU/RL)

=> s cancer? or neoplas? or tumor?
        426535 CANCER?
        595449 NEOPLAS?
        567864 TUMOR?
L3      944758 CANCER? OR NEOPLAS? OR TUMOR?

=> s l2 (L) l3
L4          99 L2 (L) L3

=> s l4 not py>1998
      11906794 PY>1998
L5          21 L4 NOT PY>1998

=> d ibib abs 1-5

L5   ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        1998:696531  CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER:         130:61153
TITLE:                   The role of vitamin D3 and antiestrogens in modulating
```

apoptosis of breast cancer cells and tumors
AUTHOR(S): Welsh, JoEllen; Van Weelden, Kathryn; Flanagan, Louise; Byrne, Ian; Nolan, Elizabeth; Narvaez, Carmen J.
CORPORATE SOURCE: W. Alton Jones Cell Science Center, Lake Placid, NY, 12946, USA
SOURCE: Subcellular Biochemistry (1998), 30, 245-270
CODEN: SBCBAG; ISSN: 0306-0225
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.50 refs. with the following key sections: overview of apoptosis; vitamin D3 as a neg. growth regulator of breast cancer cells; interactions between vitamin D3 and estrogens in breast cancer cells, including complementary effects with antiestrogens; synthetic vitamin D3 analogs; and summary and perspectives.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:566558 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 129:270193
ORIGINAL REFERENCE NO.: 129:54917a
TITLE: Novel vitamin D3 analog (CB1093) when combined with paclitaxel and cisplatin inhibit growth of MCF-7 human breast cancer cells in vivo
AUTHOR(S): Koshizuka, Kozo; Koike, Michiaki; Kubota, Tetsuya; Said, Jonathan; Binderup, Lise; Koeffler, H. Phillip
CORPORATE SOURCE: Division of Hematology/Oncology and Division of Pathology, Department of Medicine, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA, 90048, USA
SOURCE: International Journal of Oncology (1998), 13(3), 421-428
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vitamin D3 compds. paclitaxel (Taxol) and cisplatin (CDDP, cis-diamminodichloroplatinum) inhibit growth of a variety of malignant cells. The ability was examined of a novel 20-epi-vitamin D3 analog (code name, CB 1093), Taxol, and CDDP either alone or in combination to inhibit the growth of a human mammary cancer (MCF-7) growing in BNX triple immunodeficient mice. Tumors in control animals demonstrated infiltrating poorly differentiated adenocarcinomas. At the doses chosen, the antitumor effect of Taxol alone was greater than that of either CB 1093 or CDDP alone; and additive effects were observed when either CB 1093 + Taxol or CB 1093 + CDDP + Taxol were administered together. The combination of CB 1093 + Taxol + CDDP was most potent, inhibiting tumor wts. by nearly 83% compared to control tumors and producing extensive necrosis of the remaining tumor mass. No additive effect occurred by combining either CB 1093 + CDDP or Taxol + CDDP compared to Taxol alone. For all cohorts, their complete hematopoietic blood counts, serum electrolyte analyses including serum Ca as well as their liver and renal functions were within the normal range. Extensive histol. analyses of the liver, spleen, kidneys, bone marrow, skin, and s.c. fat pads from these mice showed no abnormalities. In summary, combined therapy with CB 1093, Taxol, and CDDP, which have non-cross reactive toxicities, holds promise in the treatment of patients with breast cancer.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:223635 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:317616
ORIGINAL REFERENCE NO.: 128:62821a,62824a
TITLE: Regulation of transforming growth factor-β type II receptor expression in human breast cancer MCF-7 cells by vitamin D3 and its analogs
AUTHOR(S): Wu, Gengfei; Fan, Robert S.; Li, Wenhui; Srinivas, Venkateswarlu; Brattain, Michael G.
CORPORATE SOURCE: Department of Pharmacology, Dartmouth Medical School, Hanover, NH, 03755, USA
SOURCE: Journal of Biological Chemistry (1998), 273(13), 7749-7756
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In view of the tumor suppressor role of the transforming growth factor-β (TGFβ) type II receptor (RII), the identification and characterization of agents that can induce the expression of this receptor are of potential importance to the development of chemoprevention approaches as well as treatment of cancer. To date, the identification of exogenous agents that control RII expression has been rare. The authors demonstrated that proliferation of MCF-7 early passage cells (MCF-7 E), which express RII and are sensitive to TGFβ growth inhibition activity, was significantly inhibited by vitamin D3 and its analog EB1089. In contrast, proliferation of MCF-7 late passage cells (MCF-7 L), which have lost cell surface RII and are resistant to TGFβ, was not affected by these two compds. TGFβ-neutralizing antibody was able to block the inhibitory effect on MCF-7 E cells by these compds., indicating that treatment induced autocrine-neg. TGFβ activity. An RNase protection assay showed approx. a 3-fold induction of the RII mRNA, while a receptor crosslinking assay revealed a 3-4-fold induction of the RII protein. In contrast, there was no change in either RII mRNA or protein in the MCF-7 L cells.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:789485 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:84701
ORIGINAL REFERENCE NO.: 128:16421a,16424a
TITLE: Vitamin D3 and ceramide reduce the invasion of tumor cells through extracellular matrix components by elevating protein phosphatase-2A
AUTHOR(S): Metz, Raymond J.; Vellody, Kishore; Patel, Snehal; Bergstrom, Richard; Meisinger, Jeremy; Jackson, Jodi; Wright, Mark A.; Young, M. Rita I.
CORPORATE SOURCE: Department of Pathology, Loyola University Stritch School of Medicine, Maywood, IL, USA
SOURCE: Invasion & Metastasis (1997), Volume Date 1996, 16(6), 280-290
CODEN: INVMDJ; ISSN: 0251-1789
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increasing phosphorylation reactions by protein kinase A (PKA) or reducing dephosphorylation reactions of protein phosphatase-2A (PP-2A) increases the invasiveness of Lewis lung carcinoma (LLC) cells, as measured by their

capacity to traverse extracellular matrix (ECM)-coated filters. Metastatic LLC-LN7 variants have reduced PP-2A activity when compared to nonmetastatic LLC-C8 variants. Immunoblotting showed that this reduced level of PP-2A activity was not due to reduced levels of the PP-2A catalytic (C) subunit. The cellular PP-2A activity could be stimulated by addition of C2-ceramide to LLC-LN7 lysates, or by incubating cells with either C2-ceramide or with a noncalcemic analog of vitamin D3, which has previously been shown to stimulate the release of ceramide. These treatments to elevate PP-2A activity in metastatic LLC-LN7 cells resulted in a decline in their capacity to invade through select (ECM) components, particularly through vitronectin and laminin. Underscoring the importance of PP-2A in limiting the invasiveness of tumor cells was the demonstration that LLC-LN7 cell transfectants overexpressing the PP-2A Cα subunit were less invasive through ECM components than the wild-type cells. Invasion by these cells was further reduced by addnl. increasing PP-2A activity by incubation with C2-ceramide or the vitamin D3 analog. These results suggest a role of a vitamin D3/ceramide/PP-2A pathway in limiting the invasiveness of tumor cells through select ECM components.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:722070 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:490
ORIGINAL REFERENCE NO.: 128:95a,98a
TITLE: Chemoprevention of colon cancer by vitamin D3 and its metabolites/analogs
AUTHOR(S): Brasitus, Thomas A.; Sitrin, Michael D.
CORPORATE SOURCE: Dep. Med., Univ. Chicago Hospitals & Clinics, Chicago, IL, USA
SOURCE: Vitamin D (1997), 1141-1154. Editor(s): Feldman, David; Glorieux, Francis H.; Pike, J. Wesley. Academic: San Diego, Calif.
CODEN: 65GCAB
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 112 refs., which discusses: actions of 1,25-dihydroxyvitamin D3 and other metabolites/analogs of vitamin D3 in normal colonocytes and cultures colonic cancer; evidence that vitamin D3 and its metabolites/analogs may prevent development of colorectal cancer; and potential mechanisms involved in colonic chemotherapeutic and chemopreventive actions of vitamin D3 metabolites/analogs.
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 10:24:52 ON 01 JUN 2009)

FILE 'REGISTRY' ENTERED AT 10:26:16 ON 01 JUN 2009
E "VITAMIN D3"/CN 25
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 10:26:50 ON 01 JUN 2009
L2 1256 S L1/THU
L3 944758 S CANCER? OR NEOPLAS? OR TUMOR?
L4 99 S L2 (L) L3
L5 21 S L4 NOT PY>1998

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        128401 LEUKE?
L6          20 L5 NOT LEUKE?

=> s l5 not py>1997
      12704360 PY>1997
L7          17 L5 NOT PY>1997

=> d ibib abs 1-17

L7   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        1997:789485  CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER:         128:84701
ORIGINAL REFERENCE NO.:  128:16421a,16424a
TITLE:                   Vitamin D3 and ceramide reduce the invasion of tumor
                         cells through extracellular matrix components by
                         elevating protein phosphatase-2A
AUTHOR(S):               Metz, Raymond J.; Vellody, Kishore; Patel, Snehal;
                         Bergstrom, Richard; Meisinger, Jeremy; Jackson, Jodi;
                         Wright, Mark A.; Young, M. Rita I.
CORPORATE SOURCE:        Department of Pathology, Loyola University Stritch
                         School of Medicine, Maywood, IL, USA
SOURCE:                  Invasion & Metastasis (1997), Volume Date 1996, 16(6),
                         280-290
                         CODEN: INVMDJ; ISSN: 0251-1789
PUBLISHER:               S. Karger AG
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Increasing phosphorylation reactions by protein kinase A (PKA) or reducing
     dephosphorylation reactions of protein phosphatase-2A (PP-2A) increases
     the invasiveness of Lewis lung carcinoma (LLC) cells, as measured by their
     capacity to traverse extracellular matrix (ECM)-coated filters.
     Metastatic LLC-LN7 variants have reduced PP-2A activity when compared to
     nonmetastatic LLC-C8 variants.  Immunoblotting showed that this reduced
     level of PP-2A activity was not due to reduced levels of the PP-2A
     catalytic (C) subunit.  The cellular PP-2A activity could be stimulated by
     addition of C2-ceramide to LLC-LN7 lysates, or by incubating cells with
     either C2-ceramide or with a noncalcemic analog of vitamin D3, which has
     previously been shown to stimulate the release of ceramide.  These
     treatments to elevate PP-2A activity in metastatic LLC-LN7 cells resulted
     in a decline in their capacity to invade through select (ECM) components,
     particularly through vitronectin and laminin.  Underscoring the importance
     of PP-2A in limiting the invasiveness of tumor cells was the demonstration
     that LLC-LN7 cell transfectants overexpressing the PP-2A Cα subunit
     were less invasive through ECM components than the wild-type cells.
     Invasion by these cells was further reduced by addnl. increasing PP-2A
     activity by incubation with C2-ceramide or the vitamin D3 analog.  These
     results suggest a role of a vitamin D3/ceramide/PP-2A pathway in limiting
     the invasiveness of tumor cells through select ECM components.
REFERENCE COUNT:         38    THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 2 OF 17  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        1997:722070  CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER:         128:490
ORIGINAL REFERENCE NO.:  128:95a,98a
TITLE:                   Chemoprevention of colon cancer by vitamin D3 and its
                         metabolites/analogs
AUTHOR(S):               Brasitus, Thomas A.; Sitrin, Michael D.
CORPORATE SOURCE:        Dep. Med., Univ. Chicago Hospitals & Clinics, Chicago,
                         IL, USA
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SOURCE: Vitamin D (1997), 1141-1154. Editor(s): Feldman, David; Glorieux, Francis H.; Pike, J. Wesley. Academic: San Diego, Calif.
CODEN: 65GCAB
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 112 refs., which discusses: actions of 1,25-dihydroxyvitamin D3 and other metabolites/analogs of vitamin D3 in normal colonocytes and cultures colonic cancer; evidence that vitamin D3 and its metabolites/analogs may prevent development of colorectal cancer; and potential mechanisms involved in colonic chemotherapeutic and chemopreventive actions of vitamin D3 metabolites/analogs.
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:722060 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:10003
ORIGINAL REFERENCE NO.: 128:1865a,1868a
TITLE: Vitamin D: anticancer agent and differentiation inducer
AUTHOR(S): van Leeuwen, Johannes P. T. M.; Pols, Huibert A. P.
CORPORATE SOURCE: Dep. Internal Med. III, Erasmus Univ. Med. Sch., Rotterdam, Neth.
SOURCE: Vitamin D (1997), 1089-1105. Editor(s): Feldman, David; Glorieux, Francis H.; Pike, J. Wesley. Academic: San Diego, Calif.
CODEN: 65GCAB
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 199 refs.
REFERENCE COUNT: 199 THERE ARE 199 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:710359 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:180
ORIGINAL REFERENCE NO.: 128:35a,38a
TITLE: Vitamin D inhibits telomerase activity and tumor cell invasion in human prostate cancer LNCaP cells
AUTHOR(S): Landman, Jaime; Kotkin, Adam M.; Shu, Wei-Ping; Droller, Michael J.; Liu, Brian C. -S.
CORPORATE SOURCE: Department of Urology, Mount Sinai School of Medicine, New York, NY, USA
SOURCE: Surgical Forum (1997), 48, 758-761
CODEN: SUFOAX; ISSN: 0071-8041
PUBLISHER: American College of Surgeons
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the less aggressive prostate cancer LNCaP cells, vitamin D3 decreased proliferation and induced differentiation determined as telomerase activity and prostate-specific antigen. In contrast, vitamin D3 had no effect in the more aggressive human prostate cancer cell line PPC-1. This suggests a possible role for vitamin D3 in the clin. management of a subset of human prostate cancers.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:679355 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:355620
ORIGINAL REFERENCE NO.: 127:69543a,69546a
TITLE: Effects of vitamin D3 on proliferation of cancer cells in vitro
AUTHOR(S): Fife, R. S.; Sledge, , G. W. Jr.; Proctor, C.
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1997), 120(1), 65-69
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The principal cause of death from most forms of cancer is metastatic disease. Cancer cells appear to grow quickly out of the control of the normal host regulatory mechanisms. Many factors contribute to this unrestrained proliferation, including increased metalloproteinase activity causing degradation of the extracellular matrix surrounding cancer cells, angiogenesis permitting easy access of the cells to the bloodstream and decrease or loss of programmed cell death, or apoptosis, an important mechanism for removal of abnormal or senescent cells. Treatment modalities targeted towards arresting cancer cell proliferation and spread are needed to improve the survival of patients with cancer. Vitamin D3, 1,25-dihydroxycholecalciferol D3, has been shown to induce apoptosis in the human breast cancer cell line, MCF-7. The authors have studied the effects of three concns. of vitamin D3 on the human breast cancer cell line, MDA-MB-435, the human prostate cancer cell line, LNCaP, and a human osteosarcoma cell line, U2OS. The authors report that vitamin D3 strikingly inhibits cell proliferation and induces apoptosis in all three cell lines.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:533277 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:242795
ORIGINAL REFERENCE NO.: 127:47211a,47214a
TITLE: Inhibition of proliferation of prostate cancer cells by a 19-nor-hexafluoride vitamin D3 analog involves the induction of p21waf1, p27kip1 and E-cadherin
AUTHOR(S): Campbell, M. J.; Elstner, E.; Holden, S.; Uskokovic, M.; Koeffler, H. P.
CORPORATE SOURCE: Div. Hematol./Oncol., Cedars-Sinai Med. Cent., UCLA Sch. Med., Los Angeles, CA, 90048, USA
SOURCE: Journal of Molecular Endocrinology (1997), 19(1), 15-27
CODEN: JMLEEI; ISSN: 0952-5041
PUBLISHER: Journal of Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have synthesized and studied the ability of a series of seven novel 1α,25(OH)2vitamin D3 analogs to inhibit clonal growth of prostate cancer cells (LNCaP, PC-3 and DU-145). Addition of double and triple bonds to the C/D ring (C-16) and side chain (C-22 and C-23) as well as lengthening of the side chain were important for enhanced activity against LNCaP and PC-3. Reorientation of the side chain in the 20-epi configuration resulted in analogs that were extremely potent only against LNCaP (ED50 ≈5 + 10-11 M). Compds. with six fluorines on the end of the side chain were very active against both PC-3 and LNCaP (ED50 ≈2 + 10-8 M). DU-145 cells were relatively resistant

to compds. with all of these modifications, but removal of C-19 (e.g. 1,25(OH)2-16-ene-23-yne-26,27-F6-19-nor-D3) resulted in an analog that was inhibitory against all three prostate cell lines. Further anal. showed that pulse exposure (3 days, 10-7 M) to this analog was enough to inhibit clonal growth of PC-3 cells by 50%. The same exposure also induced cell cycle arrest of all three cell lines, accompanied by upregulated protein expression of the cyclin-dependent kinase inhibitor (CDKI) known as p21waf1 in all three cell lines, and the CDKI known as p27kip1in LNCaP cells. Associated with upregulation of these CDKIs, partial differentiation occurred as measured by increased expression of both prostate-specific antigen by LNCaP cells and E-cadherin, a cell adhesion protein that may act as a putative tumor suppressor (LNCaP and PC-3 cells). In summary, this is the first report of a potent series of 19-nor-vitamin D3 analogs with the ability to inhibit proliferation of LNCaP, PC-3 and DU-145 prostate cancer cell lines. These compds. may mediate their potent anti-proliferative activities through a cell cycle arrest pathway.

L7 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:83955 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 126:117296
ORIGINAL REFERENCE NO.: 126:22641a,22644a
TITLE: 20-Epi-vitamin D3 analogs: Potent modulators of proliferation and differentiation of breast cancer cell lines in vitro
AUTHOR(S): Elstner, E.; Heber, D.; Koeffler, H. P.
CORPORATE SOURCE: School Medicine, UCLA, Los Angeles, CA, 90048, USA
SOURCE: Advances in Experimental Medicine and Biology (1996), 399(Dietary Fats, Lipids, Hormones, and Tumorigenesis), 53-70
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and book chapter with 125 refs. Breast cancer is a devastating disease. New approach in therapy are needed. In this chapter, we describe our efforts to identify novel vitamin D3 analogs which may have a potent antiproliferative effect on breast cancer without causing hypercalcemia.

L7 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:330598 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 125:48554
ORIGINAL REFERENCE NO.: 125:9053a,9056a
TITLE: Vitamin D3 treatment of tumor bearers can stimulate immune competence and reduce tumor growth when treatment coincides with a heightened presence of natural suppressor cells
AUTHOR(S): Young, M. Rita I.; Lozano, Yvonne; Ihm, Joe; Wright, Mark A.; Prechel, M. Margaret
CORPORATE SOURCE: Research Service (151-Z2), Hines VA Hospital, Hines, IL, 60141, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1996), 104(2), 153-161
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By secreting granulocyte-macrophage colony-stimulating factor (GM-CSF), Lewis lung carcinoma tumors induce immune suppressive granulocyte-macrophage progenitor cells. Treating mice having established tumors and high levels of suppressor activity with vitamin D3 eliminated

suppressor activity, increased anti-tumor immunity, induced an immune stimulatory cell population, and reduced tumor growth. When instead, the vitamin D3 treatment was initiated earlier, when implanted tumors first became detectable and when natural suppressor activity was less prominent, the treatment had no effect. Thus, vitamin D3 treatment can stimulate the immune competence of tumor bearers when treatment is targeted to coincide with a heightened presence of GM-CSF-induced suppressor cells.

L7 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:261052 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 124:331387
ORIGINAL REFERENCE NO.: 124:61133a,61136a
TITLE: Chemoprevention of breast cancer
AUTHOR(S): Ikeda, Tadashi; Sakata, Michio
CORPORATE SOURCE: Sch. Med., Keio Univ., Tokyo, 160, Japan
SOURCE: Molecular Medicine (Tokyo) (1996), 33(4), 450-6
CODEN: MOLMEL; ISSN: 0918-6557
PUBLISHER: Nakayama Shoten
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 19 refs., on the use of green tea extract, Ca, oltipraz, dehydroepiandrosterone3 and D2, tamoxifen, retinoids and N-(4-hydroxyphenyl)retinamide as chemopreventive drugs for breast cancer.

L7 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:826431 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:245881
ORIGINAL REFERENCE NO.: 123:43619a,43622a
TITLE: Control of malignant tumor with vitamin D
AUTHOR(S): Inaba, Masaaki
CORPORATE SOURCE: Med. Sch., Osaka City Univ., Osaka, 545, Japan
SOURCE: Clinical Calcium (1995), 5(9), 1179-82
CODEN: CLCCEJ; ISSN: 0917-5857
PUBLISHER: Iyaku Janarusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 5 refs., on effect of vitamin D on malignant tumor and chemical structures, physiol. activities, and in vitro and in vivo antitumor activities of 24-homo- and 26,27-hexafluoro-1,25-dihydroxyvitamin D3.

L7 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:724022 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:133717
ORIGINAL REFERENCE NO.: 123:23557a,23560a
TITLE: Vitamin-D3 derivatives and breast-tumor cell growth: effect on intracellular calcium and apoptosis
AUTHOR(S): Vandewalle, Brigitte; Hornez, Louis; Wattez, Nicole; Revillion, Francoise; Lefebvre, Jean
CORPORATE SOURCE: Laboratoire d'Endocrinologie Experimentale, Centre Oscar Lambret, Lille, 59020, Fr.
SOURCE: International Journal of Cancer (1995), 61(6), 806-11
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vitamin-D3 derivs. are now well-recognized growth inhibitors of numerous tumoral cells and in particular breast-cancer cells. However, the mechanisms by which they operate are not well established. Among the wide range of physiol. and biol. functions of vitamin-D3 derivs., the best described include their action on calcium homeostasis. In this study, the authors sought to establish whether the effects of vitamin-D3 derivs. on breast-cancer cell growth may be in part related to intracellular calcium

modulation and induction of apoptosis. To address these questions, the authors used, in addition to 1,25(OH)2D3, the active metabolite of vitamin D3, a non-calcemic 1,25(OH)2D3 derivative: Ro 23-7553 [16-ene-23-yne-1,25(OH)2D3], which in their hands was more potent than the parent compound in inhibiting breast-cancer cell growth. The authors showed that the efficiency of both compds. in growth inhibition was higher in the estradiol-receptor-pos.-breast-tumor MCF-7 cells than in the estradiol-receptor-neg. MDA-MB 231 cells. In MCF-7 cells in particular, important modifications of intracellular calcium related to the emptying of intracellular pools were observed The depletion of Ca++ from intracellular stores was followed by the induction of apoptosis. Such a phenomenon was never observed in MDA-MB 231 cells. The results suggest that the action of vitamin-D3 derivs. on the depletion of calcium stores, which was more significant in MCF-7 than in MDA-MB 231 cells, may induce apoptosis in the former cells and account for the high efficiency of vitamin-D3 derivs. on growth inhibition of MCF-7 breast-tumor cells.

L7 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:706189 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:161603
ORIGINAL REFERENCE NO.: 123:28571a,28574a
TITLE: Synergistic inhibition of breast cancer cell growth by vitamin D3 analogs and tamoxifen
AUTHOR(S): Vink-Van Wijngaarden, Trudy; Pols, Huibert A. P.; Binderup, Lise; Buurman, Cok J.; Van Den Bemd, Gert-Jan C. M.; Birkenhager, Jan C.; Van Leeuwen, Johannes P. T. M.
CORPORATE SOURCE: Department Internal Medicine III, Erasmus University, Rotterdam, Neth.
SOURCE: Proceedings of the Workshop on Vitamin D (1994), 9th(Vitamin D), 504-5
CODEN: PWVDDU; ISSN: 0721-7110
PUBLISHER: de Gruyter
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors examined the antiproliferative effects of three vitamin D3 analogs (CB966, EB1089, KH1060) in combination with the antiestrogen tamoxifen on human breast cancer cells in culture. The complimentary growth inhibition observed for tamoxifen and the vitamin D3 compds. in vitro in MCF-7 cells could result in more beneficial growth response in vivo. Moreover the synergism could have the advantage that lower dosages of 1,25-(OH)2D3/analogs can be used with reduced neg. effects.

L7 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:674687 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:217449
ORIGINAL REFERENCE NO.: 123:38381a
TITLE: Vitamin D3 derivatives and breast cancer
AUTHOR(S): Colston, K. W.; Mackay, A. G.; James, S. Y.
CORPORATE SOURCE: Med. Sch., St. George's Hosp., London, SW17 0RE, UK
SOURCE: Ernst Schering Research Foundation Workshop (1995), 14, 201-24
CODEN: ESRWEL; ISSN: 0947-6075
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with many refs. on the treatment of breast cancer with vitamin D3 derivs., giving results with EB1089.

L7 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:491327 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 122:281655

ORIGINAL REFERENCE NO.: 122:51075a,51078a
TITLE: Preclinical efficacy evaluation of potential chemopreventive agents in animal carcinogenesis models: methods and results from the NCI Chemoprevention Drug Development Program
AUTHOR(S): Steele, Vernon E.; Moon, Richard C.; Lubet, Ronald A.; Grubbs, Clinton J.; Reddy, Bandaru S.; Wargovich, Michael; McCormick, David L.; Pereira, Michael A.; Crowell, James A.; et al.
CORPORATE SOURCE: DCPC, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Cellular Biochemistry (1994), (Suppl. 20), 32-54
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the NCI, Chemoprevention Branch drug development program, potential chemopreventive agents are evaluated for efficacy against chemical carcinogen-induced tumors in animal models. This paper summarizes the results of 144 agents in 352 tests using various animal efficacy models. Of these results, 146 were pos., representing 85 different agents. The target organs selected for the animals model are representative of high-incidence human cancers. The assays include inhibition of tumors induced by MNU in hamster trachea, DEN in hamster lung, AOM in rat colon (including inhibition of AOM-induced aberrant crypts), MAM in mouse colon, DMBA and MNU in rat mammary glands, DMBA promoted by TPA in mouse skin, and OH-BBN in mouse bladder. The agents tested may be classified into various pharmacol. and chemical structural categories that are relevant to their chemopreventive potential. These categories include antiestrogens, antiinflammatories (e.g., NSAIDs), antioxidants, arachidonic acid metabolism inhibitors, GST and GSH enhancers, ODC inhibitors, protein kinase C inhibitors, retinoids and carotenoids, organosulfur compds., calcium compds., vitamin D3 and analogs, and phenolic compds. (e.g., flavonoids). The various categories of compds. have different spectra of efficacy in animal models. In hamster lung, GSH-enhancing agents and antioxidants appear to have high potential for inhibiting carcinogenesis. In the colon, NSAIDs and other antiinflammatory agents appear particularly promising. Likewise, NSAIDs are very active in mouse bladder. In rat mammary glands, retinoids and antiestrogens (as would be expected) are efficacious. Several of the chems. evaluated also appear to eb promising chemopreventive agents based on their activity in several of the animal models. Particularly, the ODC inhibitor DFMO was active in the colon, mammary glands, the bladder models, while the dithiolthione, oltipraz, was efficacious in all the models listed above (i.e., lung, colon, mammary glands, skin, and bladder).

L7 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:326434 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 122:96002
ORIGINAL REFERENCE NO.: 122:17899a,17902a
TITLE: Actions of vitamin D3 analogs on human prostate cancer cell lines: comparison with 1,25-dihydroxyvitamin D3
AUTHOR(S): Skowronski, Roman J.; Peehl, Donna M.; Feldman, David
CORPORATE SOURCE: Dep. Med. and Urology (D.M.P.), Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: Endocrinology (1995), 136(1), 20-6
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Data from epidemiol. studies has suggested that vitamin D deficiency may promote prostate cancer, although the mechanism is not understood. The authors have previously demonstrated the presence of vitamin D receptors (VDR) in three human prostate carcinoma cell lines (LNCaP, PC-3, and DU-145) as well as in primary cultures of stromal and epithelial cells derived from normal and malignant prostate tissues. The authors have also shown that 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] can elicit an antiproliferative action in these cells. In the present study the authors compared the biol. actions of 1,25-(OH)2D3 to those of a series of natural vitamin D3 metabolites and several synthetic analogs of vitamin D3 known to exhibit less hypercalcemic activity in vivo. In ligand binding competition expts., the authors demonstrated the following order of potency in displacing [3H]1,25-(OH)2D3 from VDR: EB-1089 > 1,25-(OH)2D3 > MC-903 > 1,24,25(OH)3D3 > 22-oxacalcitriol (OCT) > 1α,25-dihydroxy-16-ene-cholecalciferol (Ro 24-2637) > 25-hydroxyvitamin D3, with EB-1089 being .apprx.2-fold more potent than the native hormone. No competitive activity was found for 25-hydroxy-16,23-diene-cholecalciferol. When compared for ability to inhibit proliferation of LNCaP cells, MC-903, EB-1089, OCT, and Ro 24-2637 exhibited 4-, 3-, 3-, and 2-fold greater inhibitory activity than 1,25-(OH)2D3. Interestingly, although OCT and Ro 24-2637 exhibit, resp., 10 and 14 times lower affinity for VDR than 1,25-(OH)2D3, both compds. inhibited the proliferation of LNCaP cells with a potency greater than that of the native hormone. The relative potency of vitamin D3 metabolites and analogs to inhibit cell proliferation correlated well with the ability of these compds. to stimulate prostate-specific antigen secretion by LNCaP cells as well as with their potency to induce the 25-hydroxyvitamin D3-24-hydroxylase mRNA transcript in PC-3 cells. In conclusion, these results demonstrate that synthetic analogs of vitamin D3, known to exhibit reduced calcemic activity, can elicit antiproliferative effects and other biol. actions in LNCaP and PC-3 cell lines. It is noteworthy that although binding to VDR is critical for 1,25-(OH)2D3 action, the analog data indicate that addnl. factors significantly contribute to the magnitude of the biol. response. Finally, the strong antiproliferative effects of several synthetic analogs known to exhibit less calcemic activity than 1,25-(OH)2D3 suggest that these compds. potentially may be useful as an addnl. therapeutic option for the treatment of prostate cancer.

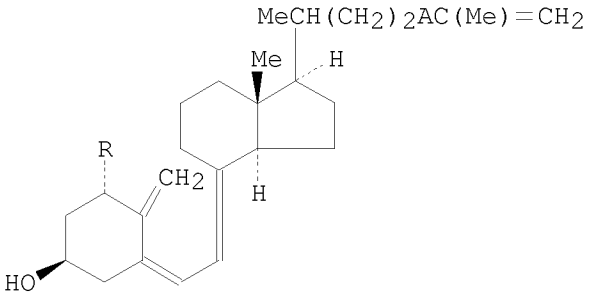
L7 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:196237 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 122:515
ORIGINAL REFERENCE NO.: 122:111a,114a
TITLE: Inhibition of breast cancer cell growth by combined treatment with vitamin D3 analogs and tamoxifen
AUTHOR(S): Wijngaarden, Trudy Vink-van; Pols, Huibert A. P.; Buurman, Cok J.; van den Bemd, Gert Jan C. M.; Dorssers, Lambert C. J.; Birkenhaeger, Jan C.; van Leeuwen, Johannes P. T. M.
CORPORATE SOURCE: Dep. Internal Med. III, Erasmus Univ., Rotterdam, Neth.
SOURCE: Cancer Research (1994), 54(21), 5711-17
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The steroid hormone 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] has potential to be used as an antitumor agent, but its clin. application is restricted by the strong calcemic activity. Therefore, new vitamin D3 analogs are developed with increased growth inhibitory and reduced calcemic activity. In the present study, we have examined the antiproliferative effects of four

novel vitamin D3 analogs (CB966, EB1089, KH1060, and 22-oxa-calcitriol) on breast cancer cells, either alone or in combination with the antiestrogen tamoxifen. The estrogen-dependent ZR-75-1 and estrogen-responsive MCF-7 cell lines were used as a model. It was shown that, with EB1089 and KH1060, the same growth inhibitory effect as 1,25-(OH)2D3 could be reached at up to 100-fold lower concns., whereas CB966 and 22-oxa-calcitriol were nearly equipotent with 1,25-(OH)2D3. The growth inhibition by the vitamin D3 compds. could be augmented by combined treatment with tamoxifen. At the maximal effective concns. of the vitamin D3 compds., the effect of combined treatment was additive (MCF-7 cells) or less than additive (ZR-75-1 cells). Tamoxifen increased the sensitivity of the cells to the vitamin D3 compds. 2- to 4000-fold, which was expressed by a shift to lower median effective concentration values. Thereby, the vitamin D3 compds. may be used at even lower dosages in combination therapy with tamoxifen. A major problem of tamoxifen therapy is the development of tamoxifen resistance. Together, our data point to a potential benefit of combination therapy with 1,25-(OH)2D3 or vitamin D3 analogs and tamoxifen for the treatment of breast cancer.

L7 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1985:529054 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 103:129054
ORIGINAL REFERENCE NO.: 103:20563a,20566a
TITLE: 25-Dehydrovitamin D3 derivatives as neoplasm inhibitors
PATENT ASSIGNEE(S): Teijin Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60067422	A	19850417	JP 1983-174356	19830922

PRIORITY APPLN. INFO.: JP 1983-174356 19830922
GI



I

AB 25-Dehydrovitamin D3 derivs. I (R = H or OH; A = carbonyl or hydroxymethylene) are neoplasm inhibitors. Thus, 24-oxo-5α,8α-(4-phenyl-1,2-urazolo)cholest-6-ene-1α,3β-diol [96862-44-1] was prepared by the treatment of

24-oxocholesta-5,7-diene-1α-,3β-diol [70834-97-8] with
4-phenyl-1,2,4-triazoline-3,5-dione [4233-33-4].
24-Oxo-25-dehydro-1α-hydroxyvitamin D3 [95420-03-4] was dissolved
in coconut oil (7 μg/mL) and encapsulated with a solution consisting of
gelatin, glycerin, Et 4-hydroxybenzoate, and H2O. I pharmacol. studies
were described.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	89.68	95.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-18.04	-18.04

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=> E "CALCIDIOL"/CN 25

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E2	1	CALCIDIA/CN
E3	1 -->	CALCIDIOL/CN
E4	1	CALCIDIOL 24-HYDROXYLASE/CN
E5	1	CALCIDIOL 3-HEMISUCCINATE/CN
E6	1	CALCIDIOL LACTONE/CN
E7	1	CALCIDIOL LACTONE, (23R)-/CN
E8	1	CALCIDOL/CN
E9	1	CALCIE F 2000/CN
E10	1	CALCIE F 6401/CN
E11	1	CALCIE F 6402/CN
E12	1	CALCIE F 9850/CN
E13	1	CALCIFEDIOL/CN
E14	1	CALCIFERIN/CN
E15	1	CALCIFEROL/CN
E16	1	CALCIFEROL 25-HYDROXYLASE/CN
E17	1	CALCIFEROL PHOSPHATE/CN
E18	1	CALCIFEROL PROPIONATE/CN

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E19          1     CALCIFEROL SULFOTRANSFERASE/CN
E20          1     CALCIFEROL-WARFARIN MIXT./CN
E21          1     CALCIFICATION ASSOCIATED SOLUBLE MATRIX PROTEIN 2 (PROCAMBARUS
CLARKII GENE CASP-2)/CN
E22          1     CALCIFICATION-ASSOCIATED PEPTIDE-1 (PROCAMBARUS CLARKII GENE
CAP-1)/CN
E23          1     CALCIFICATION-ASSOCIATED PEPTIDE-2 (PROCAMBARUS CLARKII GENE
CAP-2)/CN
E24          1     CALCIFIED CUTICLE PROTEIN (CALLINECTES SAPIDUS GENE CP8.2)/CN
E25          1     CALCIFIED CUTICLE PROTEIN (CALLINECTES SAPIDUS GENE CP8.5)/CN

=> S E3
L8           1 CALCIDIOL/CN

=> DIS L8 1 SQIDE
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L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   19356-17-3  REGISTRY
CN   1H-Indene-1-pentanol, 4-[(2Z)-2-[(5S)-5-hydroxy-2-
     methylenecyclohexylidene]ethylidene]octahydro-α,α,ε,7a-
     tetramethyl-, (εR,1R,3aS,4E,7aR)-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI)
CN   9,10-Secocholesta-5,7,10(19)-triene-3β,25-diol (8CI)
OTHER NAMES:
CN   25-HCC
CN   25-Hydroxycholecalciferol
CN   25-Hydroxyvitamin D
CN   25-Hydroxyvitamin D3
CN   5,6-cis-25-Hydroxyvitamin D3
CN   Calcidiol
CN   Calcifediol
CN   Calderol
CN   Cholecalciferol, 25-hydroxy-
CN   Dedrogyl
CN   Didrogyl
CN   Hidroferol
CN   Hy-D
CN   Ro 8-8892
CN   Rovimix Hy-D
CN   U 32070E
FS   STEREOSEARCH
DR   25631-40-7
MF   C27 H44 O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU,
       EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
       NAPRALERT, PROMT, PS, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL,
       USPATOLD, VETU
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent; Report
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
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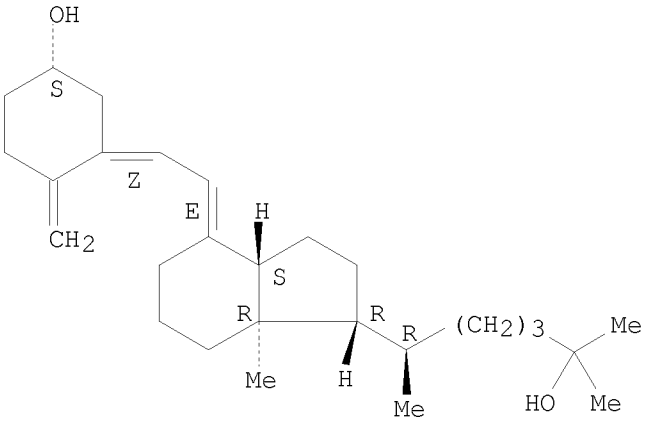
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.



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49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3526 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FULL ESTIMATED COST	7.88	103.83

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CA SUBSCRIBER PRICE	0.00	-18.04

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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

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FILE 'REGISTRY' ENTERED AT 10:26:16 ON 01 JUN 2009
E "VITAMIN D3"/CN 25
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 10:26:50 ON 01 JUN 2009
L2 1256 S L1/THU
L3 944758 S CANCER? OR NEOPLAS? OR TUMOR?
L4 99 S L2 (L) L3
L5 21 S L4 NOT PY>1998
L6 20 S L5 NOT LEUKE?
L7 17 S L5 NOT PY>1997

FILE 'REGISTRY' ENTERED AT 10:36:16 ON 01 JUN 2009
E "CALCIDIOL"/CN 25
L8 1 S E3

FILE 'CAPLUS' ENTERED AT 10:37:04 ON 01 JUN 2009

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L9 3526 L8

=> s l9 and l3
L10 219 L9 AND L3

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L11 59 L10 NOT PY>1997

=> d ibib kwic

L11 ANSWER 1 OF 59 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:775344 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:71132
ORIGINAL REFERENCE NO.: 128:13783a,13786a
TITLE: 1α,25-Dihydroxyvitamin D3 and a variety of its natural metabolites transcriptionally repress nuclear-factor-κB-mediated interleukin-8 gene expression
AUTHOR(S): Harant, Hanna; Andrew, Penelope J.; Reddy, G.

Satyanarayana; Foglar, Elisabeth; Lindley, Ivan J. D.
CORPORATE SOURCE: Novartis Research Institute, Vienna, A-1235, Austria
SOURCE: European Journal of Biochemistry (1997), 250(1), 63-71
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB . . . by stable transfection with an IL-8 promoter-luciferase construct containing these sequences. 1α,25-Dihydroxyvitamin D3 (calcitriol) repressed IL-8 promoter activity induced by tumor necrosis factor-α (TNF-α) by 50%, compared to 30% inhibition using dexamethasone, an effect consistent with its effect on TNF-α-induced IL-8. . .

IT Tumor necrosis factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dihydroxyvitamin D3 and natural metabolites transcriptionally repress NF-κB-mediated interleukin-8 gene expression)

IT 50-02-2, Dexamethasone 1406-16-2D, Vitamin D, metabolites 19356-17-3, Calcidiol 32222-06-3, 1α,25-Dihydroxyvitamin D3 55721-11-4 56142-94-0 71204-89-2, Calcitroic acid 74886-61-6 76338-50-6, 24-Oxo-calcitriol 77372-59-9 81203-50-1 86701-33-9 104758-88-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dihydroxyvitamin D3 and natural metabolites transcriptionally repress NF-κB-mediated interleukin-8 gene expression)

=> s l11 not (tumor necrosis)
498429 TUMOR
182476 TUMORS
554194 TUMOR
(TUMOR OR TUMORS)
155988 NECROSIS
2 NECROSISES
155990 NECROSIS
(NECROSIS OR NECROSISES)
113422 TUMOR NECROSIS
(TUMOR(W)NECROSIS)
L12 54 L11 NOT (TUMOR NECROSIS)

=> d ibib abs kwic

L12 ANSWER 1 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:723573 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 128:33034
ORIGINAL REFERENCE NO.: 128:6457a,6460a
TITLE: Vitamin D metabolism in human colon adenocarcinoma-derived Caco-2 cells: expression of 25-hydroxyvitamin D3-1α-hydroxylase activity and regulation of side-chain metabolism
AUTHOR(S): Cross, Heide S.; Peterlik, Meinrad; Reddy, G. Satyanarayana; Schuster, Inge
CORPORATE SOURCE: Department of General and Experimental Pathology, University of Vienna Medical School, Vienna, A-1090, Austria
SOURCE: Journal of Steroid Biochemistry and Molecular Biology

(1997), 62(1), 21-28
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1α,25-Dihydroxyvitamin D3 (1α,25(OH)2D3) and its synthetic analogs exhibit structure-related variations in their growth inhibitory actions in human colon adenocarcinoma-derived Caco-2 cells. Because this might be caused by differences in resistance against metabolic degradation, we used HPLC anal. to investigate pathways of vitamin D metabolism in two different Caco-2 cell clones. Importantly, when Caco-2 cells were incubated with tritium-labeled 25-hydroxyvitamin D3 (25(OH)D3) for up to 2 h they produced almost exclusively a metabolite, which was identified as 1α,25(OH)2D3 by co-chromatog. with the synthetic standard in two different HPLC systems, and by a radioligand assay showing an identical binding affinity to the intestinal nuclear vitamin D receptor. Expression of the 25(OH)D3-1α-hydroxylase appears to be constitutive because almost identical enzyme activities are observed in any growth phase. 1α,25(OH)2D3 can also activate side chain metabolism in Caco-2 cells: thereby, 1α,25(OH)2D3 or 25(OH)D3 are metabolized through the C-24 oxidative pathway into 1α,24(R),25(OH)3D3 and 24(R),25(OH)2D3, resp., which undergo sequential metabolism into 1α,25(OH)2-24-oxo-D3 and 24-oxo-25(OH)D3. Through C-23 oxidation these intermediary metabolites are further converted into 1α,23,25(OH)3-24-oxo-D3 and 23,25(OH)2-24-oxo-D3. Also direct C-23 oxidation of the substrates 1α,25(OH)2D3 and 25(OH)D3 generates 1α,23(S),25(OH)3D3 and 23(S),25(OH)2D3, resp. In summary, our results demonstrated the presence of distinct pathways of vitamin D metabolism in Caco-2 cells: apart from metabolizing 1α,25(OH)2D3 along the C-24 and C-23 oxidative pathways, Caco-2 cells are able to synthesize 1α,25(OH)2D3 from 25(OH)D3 through constitutive expression of 25(OH)D3-1α-hydroxylase activity. The relevance of this finding for the intrinsic growth control of neoplastic colonocytes is discussed.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB . . . 1α,25(OH)2D3 from 25(OH)D3 through constitutive expression of 25(OH)D3-1α-hydroxylase activity. The relevance of this finding for the intrinsic growth control of neoplastic colonocytes is discussed.
IT Intestine, neoplasm
(colon, adenocarcinoma; vitamin D metabolism in human colon adenocarcinoma-derived Caco-2 cells and expression of 25-hydroxyvitamin D3-1α-hydroxylase activity and regulation of side-chain metabolism)
IT 19356-17-3, 25-Hydroxyvitamin D3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitamin D metabolism in human colon adenocarcinoma-derived Caco-2 cells and expression of 25-hydroxyvitamin D3-1α-hydroxylase activity and regulation of side-chain metabolism)

=> d ibib abs kwic 2

L12 ANSWER 2 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:593943 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:242931
ORIGINAL REFERENCE NO.: 127:47247a,47250a
TITLE: Synergistic induction of HL60 cell differentiation by ketoconazole and 1-desoxy analogs of vitamin D3
AUTHOR(S): Wang, Xuening; Gardner, Jeffrey P.; Kheir, Ahmed; Uskokovic, Milan R.; Studzinski, George P.

CORPORATE SOURCE: Department of Pathology & Laboratory Medicine, UMDNJ-New Jersey Medical School, Newark, NJ, 07103, USA
SOURCE: Journal of the National Cancer Institute (1997), 89(16), 1199-1206
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The goal of differentiation therapy is to induce cancer cells to stop proliferating and to express characteristics of normal cells. Vitamin D analogs, such as the deltanoids, are being evaluated as differentiation agents in the treatment of several human cancers (e.g., myeloid leukemias); however, these compds. have a tendency to produce hypercalcemia in patients receiving therapy. A combination of a differentiation-inducing deltanoid with a compound that blocks entry of calcium into cells (e.g., ketoconazole) may offer a new approach to differentiation therapy and address the problem of hypercalcemia. We investigated whether various ketoconazole-deltanoid combinations would alter cellular differentiation or intracellular calcium homeostasis in comparison with deltanoids used alone. Cultured human leukemia HL60 cells were treated with ketoconazole-deltanoid combinations. Markers of differentiation (expression of CD11b and CD14 antigens and of non-specific esterase) were measured by flow cytometry and cytochem.; cell cycle distribution was measured by flow cytometry of propidium iodide-stained cells. Expression of differentiation-related genes was assessed by northern blotting and immunoblotting, and changes in intracellular calcium homeostasis were monitored by fluorescence anal. of fura-2-containing cells. Ketoconazole strongly potentiated the differentiating activity of the deltanoids, which exhibited low potency when used alone. Ketoconazole-deltanoid combinations had little effect on HL60 cell-cycle distribution, although the cells did stop proliferating and they differentiated. Ketoconazole-deltanoid combinations produced only minor changes in intracellular calcium homeostasis compared with changes produced by 1,25-dihydroxyvitamin D3, either alone or in combination with ketoconazole. These results suggest that ketoconazole may be useful in combination with vitamin D analogs in the differentiation therapy for myeloid leukemias.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The goal of differentiation therapy is to induce cancer cells to stop proliferating and to express characteristics of normal cells. Vitamin D analogs, such as the deltanoids, are being evaluated as differentiation agents in the treatment of several human cancers (e.g., myeloid leukemias); however, these compds. have a tendency to produce hypercalcemia in patients receiving therapy. A combination of a. . .

IT 1406-16-2D, Vitamin D, analogs 19356-17-3, Ro 8-8892 32222-06-3, Ro 21-5535 65277-42-1, Ketoconazole 124409-59-2, Ro 24-2287 124409-60-5, Ro 24-2090 165811-45-0, Ro 25-9887
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic induction of HL60 cell differentiation by ketoconazole and 1-desoxy analogs of vitamin D3)

=> d kwic

L12 ANSWER 1 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AB . . . 1α,25(OH)2D3 from 25(OH)D3 through constitutive expression

of 25(OH)D3-1α-hydroxylase activity. The relevance of this finding for the intrinsic growth control of neoplastic colonocytes is discussed.

IT Intestine, neoplasm
(colon, adenocarcinoma; vitamin D metabolism in human colon adenocarcinoma-derived Caco-2 cells and expression of 25-hydroxyvitamin D3-1α-hydroxylase activity and regulation of side-chain metabolism)

IT 19356-17-3, 25-Hydroxyvitamin D3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitamin D metabolism in human colon adenocarcinoma-derived Caco-2 cells and expression of 25-hydroxyvitamin D3-1α-hydroxylase activity and regulation of side-chain metabolism)

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     FILE 'REGISTRY' ENTERED AT 10:26:16 ON 01 JUN 2009
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L1              1 S E3

     FILE 'CAPLUS' ENTERED AT 10:26:50 ON 01 JUN 2009
L2           1256 S L1/THU
L3         944758 S CANCER? OR NEOPLAS? OR TUMOR?
L4             99 S L2 (L) L3
L5             21 S L4 NOT PY>1998
L6             20 S L5 NOT LEUKE?
L7             17 S L5 NOT PY>1997

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     FILE 'CAPLUS' ENTERED AT 10:37:04 ON 01 JUN 2009
L9           3526 S L8
L10           219 S L9 AND L3
L11            59 S L10 NOT PY>1997
L12            54 S L11 NOT (TUMOR NECROSIS)

=> s l12 and (in vivo)
        510978 VIVO
             2 VIVOS
        510979 IN VIVO
                  (VIVO OR VIVOS)
L13            4 L12 AND (IN VIVO)

=> d ibib abs kwic 1-4

L13  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         1995:326434  CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER:          122:96002
ORIGINAL REFERENCE NO.:   122:17899a,17902a
TITLE:                    Actions of vitamin D3 analogs on human prostate
                          cancer cell lines: comparison with
                          1,25-dihydroxyvitamin D3
AUTHOR(S):                Skowronski, Roman J.; Peehl, Donna M.; Feldman, David
CORPORATE SOURCE:         Dep. Med. and Urology (D.M.P.), Stanford Univ. Sch.
                          Med., Stanford, CA, 94305, USA
SOURCE:                   Endocrinology (1995), 136(1), 20-6
```

CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Data from epidemiol. studies has suggested that vitamin D deficiency may promote prostate cancer, although the mechanism is not understood. The authors have previously demonstrated the presence of vitamin D receptors (VDR) in three human prostate carcinoma cell lines (LNCaP, PC-3, and DU-145) as well as in primary cultures of stromal and epithelial cells derived from normal and malignant prostate tissues. The authors have also shown that 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] can elicit an antiproliferative action in these cells. In the present study the authors compared the biol. actions of 1,25-(OH)2D3 to those of a series of natural vitamin D3 metabolites and several synthetic analogs of vitamin D3 known to exhibit less hypercalcemic activity in vivo. In ligand binding competition expts., the authors demonstrated the following order of potency in displacing [3H]1,25-(OH)2D3 from VDR: EB-1089 > 1,25-(OH)2D3 > MC-903 > 1,24,25(OH)3D3 > 22-oxacalcitriol (OCT) > 1α,25-dihydroxy-16-ene-cholecalciferol (Ro 24-2637) > 25-hydroxyvitamin D3, with EB-1089 being .apprx.2-fold more potent than the native hormone. No competitive activity was found for 25-hydroxy-16,23-diene-cholecalciferol. When compared for ability to inhibit proliferation of LNCaP cells, MC-903, EB-1089, OCT, and Ro 24-2637 exhibited 4-, 3-, 3-, and 2-fold greater inhibitory activity than 1,25-(OH)2D3. Interestingly, although OCT and Ro 24-2637 exhibit, resp., 10 and 14 times lower affinity for VDR than 1,25-(OH)2D3, both compds. inhibited the proliferation of LNCaP cells with a potency greater than that of the native hormone. The relative potency of vitamin D3 metabolites and analogs to inhibit cell proliferation correlated well with the ability of these compds. to stimulate prostate-specific antigen secretion by LNCaP cells as well as with their potency to induce the 25-hydroxyvitamin D3-24-hydroxylase mRNA transcript in PC-3 cells. In conclusion, these results demonstrate that synthetic analogs of vitamin D3, known to exhibit reduced calcemic activity, can elicit antiproliferative effects and other biol. actions in LNCaP and PC-3 cell lines. It is noteworthy that although binding to VDR is critical for 1,25-(OH)2D3 action, the analog data indicate that addnl. factors significantly contribute to the magnitude of the biol. response. Finally, the strong antiproliferative effects of several synthetic analogs known to exhibit less calcemic activity than 1,25-(OH)2D3 suggest that these compds. potentially may be useful as an addnl. therapeutic option for the treatment of prostate cancer.
TI Actions of vitamin D3 analogs on human prostate cancer cell lines: comparison with 1,25-dihydroxyvitamin D3
AB Data from epidemiol. studies has suggested that vitamin D deficiency may promote prostate cancer, although the mechanism is not understood. The authors have previously demonstrated the presence of vitamin D receptors (VDR) in three. . . series of natural vitamin D3 metabolites and several synthetic analogs of vitamin D3 known to exhibit less hypercalcemic activity in vivo. In ligand binding competition expts., the authors demonstrated the following order of potency in displacing [3H]1,25-(OH)2D3 from VDR: EB-1089 >. . . than 1,25-(OH)2D3 suggest that these compds. potentially may be useful as an addnl. therapeutic option for the treatment of prostate cancer.
ST vitamin D3 analog prostate cancer
IT Neoplasm inhibitors
(vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)
IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(PSA (prostate-specific antigen), vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)

IT Prostate gland
(neoplasm, vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitamin D, vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)

IT 67-97-0D, Vitamin D3, analogs 19356-17-3, 25-Hydroxyvitamin D3 32222-06-3, Calcitriol 50648-94-7, 1,24,25-Trihydroxy vitamin D3 103909-75-7, 22-Oxacalcitriol 112965-21-6, MC-903 124409-58-1 124409-59-2, 9,10-Secocholesta-5,7,10(19),16,23-pentaene-3,25-diol, (3β,5Z,7E,23E)- 134404-52-7, EB-1089
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)

IT 53112-53-1, 25-Hydroxyvitamin D3-24-hydroxylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitamin D3 analog effects on human prostate cancer cell lines in comparison with 1,25-dihydroxyvitamin D3)

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:554464 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 121:154464
ORIGINAL REFERENCE NO.: 121:27900h,27901a
TITLE: Constitutive synthesis of 1,25-dihydroxyvitamin D3 by a human small cell lung cancer cell line
AUTHOR(S): Mawer, E. Barbara; Hayes, Michael E.; Heys, Sara E.; Davies, Michael; White, Anne; Stewart, M. Felicity; Smith, George N.
CORPORATE SOURCE: Bone Disease Res. Cent., Manchester Univ., Manchester, UK
SOURCE: Journal of Clinical Endocrinology and Metabolism (1994), 79(2), 554-60
CODEN: JCEMAZ; ISSN: 0021-972X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB One of 16 human small cell lung cancer cell lines examined was shown to synthesize a metabolite resembling 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3]. The NCI H82 line converted 25-hydroxyvitamin D3 (25OHD3) into a compound indistinguishable from 1,25-(OH)2D3 in 3 different high performance liquid chromatog. systems. Electron impact mass spectra for the trimethylsilylethers of the metabolite and authentic 1,25-(OH)2D3 were indistinguishable. Binding to an anti-1,25-(OH)2D3 antibody was identical for the metabolite and authentic 1,25-(OH)2D3, whereas administration to rats in vivo caused equivalent stimulation of calcium transport measured in vitro in duodenal sacs. Activity of the H82 1α-hydroxylase appears to be substrate dependent and is not stimulated by PTH, suggesting that it is similar to the enzyme expressed by activated macrophages and other cell types at extrarenal sites. Inhibition by ketoconazole indicates that, like the renal and extrarenal enzymes, the H82 enzyme is cytochrome P 450 dependent. These data indicate that the H82 small cell lung cancer cell line constitutively expresses 25-hydroxyvitamin D3-1α-hydroxylase and can synthesize 1,25-(OH)2D3.

TI Constitutive synthesis of 1,25-dihydroxyvitamin D3 by a human small cell lung cancer cell line

AB One of 16 human small cell lung cancer cell lines examined was shown to synthesize a metabolite resembling 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3]. The NCI H82 line converted 25-hydroxyvitamin D3. . . were indistinguishable. Binding to an anti-1,25-(OH)2D3 antibody was identical for the metabolite and authentic 1,25-(OH)2D3, whereas administration to rats in vivo caused equivalent stimulation of calcium transport measured in vitro in duodenal sacs. Activity of the H82 1α-hydroxylase appears to be. . . and extrarenal enzymes, the H82 enzyme is cytochrome P 450 dependent. These data indicate that the H82 small cell lung cancer cell line constitutively expresses 25-hydroxyvitamin D3-1α-hydroxylase and can synthesize 1,25-(OH)2D3.

ST small lung cancer calcitriol

IT Lung, neoplasm
(small-cell carcinoma, dihydroxyvitamin D3 formation by, of human)

IT 9081-36-1, 25-Hydroxyvitamin D3-1α-hydroxylase
RL: PROC (Process)
(expression of, by human small cell lung cancer cell line)

IT 32222-06-3, 1,25-Dihydroxyvitamin D3
RL: FORM (Formation, nonpreparative)
(formation of, by human small cell lung cancer cell line)

IT 19356-17-3, 25-Hydroxyvitamin D3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, by human small cell lung cancer cell line)

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:420828 CAPLUS <<LOGINID::20090601>>

DOCUMENT NUMBER: 119:20828

ORIGINAL REFERENCE NO.: 119:3709a,3712a

TITLE: Relationship between circulating vitamin D3 metabolites and prolactin or growth hormone levels in rat

AUTHOR(S): Mortensen, Berit; Gordeladze, Jan O.; Haug, Egil; Schjerven, Leif; Gautvik, Kaare M.

CORPORATE SOURCE: Inst. Surg. Res., Natl. Hosp., Oslo, 0317, Norway

SOURCE: Pharmacology & Toxicology (Oxford, United Kingdom) (1993), 72(3), 188-93
CODEN: PHTOEH; ISSN: 0901-9928

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have demonstrated specific receptors for 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) in a clonal (GH3) strain of rat pituitary tumor cells. It was discovered that 1,25(OH)2D3 affected the production of prolactin and growth hormone in these cells in a calcium dependent manner. These findings were the basis for a hypothesis that vitamin D3 could be involved in the regulation of pituitary hormones in vivo. To further investigate this contention, female rats were given s.c. injections of 1,25(OH)2D3, 25-hydroxyvitamin D3 (25(OH)D3) or 24,25-dihydroxyvitamin D3 (24,25(OH)3D3) three times a week for ≤12 wk. Blood samples were withdrawn after 28, 56 and 84 days of treatment and analyzed for vitamin D3 metabolites, prolactin and growth hormone, and serum ionized (free) and total calcium (Ca). Between treatment group comparisons of serum prolactin and growth hormone levels did not show significant vitamin D3 induced alterations. However, correlation matrix analyses on all variables revealed that serum level of growth hormone was significantly and inversely related to corresponding total Ca. Prolactin may be subject to a complex regulation by 1,25(OH)2D3 and free Ca2+.

AB Previous studies have demonstrated specific receptors for

1,25-dihydroxyvitamin D3 (1,25(OH)2D3) in a clonal (GH3) strain of rat pituitary tumor cells. It was discovered that 1,25(OH)2D3 affected the production of prolactin and growth hormone in these cells in a calcium. . . findings were the basis for a hypothesis that vitamin D3 could be involved in the regulation of pituitary hormones in vivo . To further investigate this contention, female rats were given s.c. injections of 1,25(OH)2D3, 25-hydroxyvitamin D3 (25(OH)D3) or 24,25-dihydroxyvitamin D3 (24,25(OH)3D3). . .

IT 67-97-0D, Vitamin D3, metabolites 19356-17-3, 25-Hydroxyvitamin D3 40013-87-4, 24,25-Dihydroxyvitamin D3
RL: BIOL (Biological study)
(GH and prolactin secretion response to)

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:180270 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 108:180270
ORIGINAL REFERENCE NO.: 108:29437a,29440a
TITLE: Analogs of the hormonal form of vitamin D and their possible use in leukemia
AUTHOR(S): DeLuca, Hector F.; Ostrem, Voula K.
CORPORATE SOURCE: Dep. Biochem., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Progress in Clinical and Biological Research (1988), 259(Nutr., Growth, Cancer), 41-55
CODEN: PCBRD2; ISSN: 0361-7742
DOCUMENT TYPE: Journal
LANGUAGE: English

AB After a review of the mol. mechanism of action of 1,25-dihydroxyvitamin D3 (1,25-(OH)2D3), its possible role in tissues not previously believed to be targets of its action, the presence of 1,25-(OH)2D3 receptors in cancer cell lines, and 1,25-(OH)2D3-induced differentiation of the stem cells of myeloid cell lines, a large analog study was concluded that suggests that specific analogs of 1,25-(OH)2D3 can be prepared that have markedly enhanced activity in promoting differentiation of HL-60 promyelocytes to benign monocytes. Lengthening the side chain of 1,25-(OH)2D3 increased the activity in HL-60 cells by 1 order of magnitude when the side chain was increased in length by 1 C. At the same time, the biol. activity of these compds. in serum Ca2+ elevation was either unchanged or diminished. Thus, lengthening the side chain may well provide a preferentially active form of vitamin D on the promyelocytes. Shortening the side chain resulted in a 10-fold loss of activity in HL-60 cells for each C removed. Furthermore, elimination of the 26- and 27-C atoms decreased the biol. activity by 100-fold. If, however, the OH was left off the side chain and small hydrocarbon side chains of Et or Iso-Pr were substituted, very high activity in HL-60 cells was achieved without activity in mobilizing Ca2+ in vivo. Therefore, these are compds. which illustrate at least in vitro specific activity in HL-60 cells.

AB . . . its possible role in tissues not previously believed to be targets of its action, the presence of 1,25-(OH)2D3 receptors in cancer cell lines, and 1,25-(OH)2D3-induced differentiation of the stem cells of myeloid cell lines, a large analog study was concluded that. . . of Et or Iso-Pr were substituted, very high activity in HL-60 cells was achieved without activity in mobilizing Ca2+ in vivo. Therefore, these are compds. which illustrate at least in vitro specific activity in HL-60 cells.

IT Neoplasm inhibitors
(leukemia, dihydroxyvitamin D3 analogs as)

IT 19356-17-3 21343-40-8 32222-06-3 32222-06-3D, 1,25-Dihydroxyvitamin D3, analogs 41294-56-8 54573-75-0 55721-11-4 56142-94-0 57333-95-6 57333-96-7 60133-18-8 90191-28-9

96840-33-4 97903-36-1 97903-37-2 103656-40-2 103764-76-7
103764-86-9 105687-81-8 107425-78-5 107425-86-5 110996-20-8
110996-21-9 110996-22-0 110996-24-2 110996-25-3 111024-90-9
111024-91-0 111024-92-1
RL: BIOL (Biological study)
(leukemia cell inhibition by, structure in relation to)

=> file reg

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E2 1 CALCITRIN/CN
E3 1 --> CALCITRIOL/CN
E4 1 CALCITRIOL 24-HYDROXYLASE/CN
E5 1 CALCITRIOL 3-HEMISUCCINATE/CN
E6 1 CALCITRIOL LACTONE/CN
E7 1 CALCITRIOL LACTONE-IGF I MIXT./CN
E8 1 CALCITRIOL TRIHYDRATE/CN
E9 1 CALCITROIC ACID/CN
E10 1 CALCIUM/CN
E11 1 CALCIUM (((1,2-DIMETHYLETHYLENE)DINITRILO)TETRAACETATO)CADMATE/CN
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(((1,2-DIMETHYLETHYLENE)DINITRILO)TETRAACETATO)CUPRATE(II)/CN
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E14 1 CALCIUM
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E15 1 CALCIUM
(((2-HYDROXYTRIMETHYLENE)DINITRILO)TETRAACETATO)CADMATE/CN

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(((2-HYDROXYTRIMETHYLENE)DINITRILO)TETRAACETATO)ZINCATE/CN
E18          1     CALCIUM
((1,2-CYCLOHEXYLENEDINITRILO)TETRAACETATO)AQUOFERRATE(III)/CN
E19          1     CALCIUM ((ETHYLENEDINITRILO)TETRAACETATO)CALCIATE/CN
E20          1     CALCIUM ((ETHYLENEDINITRILO)TETRAACETATO)CUPRATE(II)/CN
E21          1     CALCIUM ((ETHYLENEDINITRILO)TETRAACETATO)NICKELATE(II)/CN
E22          1     CALCIUM ((ETHYLENEDINITRILO)TETRAACETATO)YTTRATE(III)/CN
E23          1     CALCIUM (-)-MALATE/CN
E24          1     CALCIUM (1-VINYLHEXADECYL)SUCCINATE (1:1)/CN
E25          1     CALCIUM (3,5-DI-TERT-BUTYL-4-HYDROXYBENZYL MONOETHYL
PHOSPHONATE)/CN

=> S E3
L14          1 CALCITRIOL/CN

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(L14 (L) THU/RL)

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L16 340 L15 (L) L3

=> s prostate and l16
65580 PROSTATE
1519 PROSTATES
65691 PROSTATE
(PROSTATE OR PROSTATES)
L17 151 PROSTATE AND L16

=> s l17 not py>1998
11906794 PY>1998
L18 17 L17 NOT PY>1998

=> s l17 not py>1997
12704360 PY>1997
L19 14 L17 NOT PY>1997

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L19 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:679355 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:355620
ORIGINAL REFERENCE NO.: 127:69543a,69546a
TITLE: Effects of vitamin D3 on proliferation of cancer cells in vitro
AUTHOR(S): Fife, R. S.; Sledge, , G. W. Jr.; Proctor, C.
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1997), 120(1), 65-69
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The principal cause of death from most forms of cancer is metastatic disease. Cancer cells appear to grow quickly out of the control of the normal host regulatory mechanisms. Many factors contribute to this unrestrained proliferation, including increased metalloproteinase activity causing degradation of the extracellular matrix surrounding cancer cells, angiogenesis permitting easy access of the cells to the bloodstream and decrease or loss of programmed cell death, or apoptosis, an important mechanism for removal of abnormal or senescent cells. Treatment modalities targeted towards arresting cancer cell proliferation and spread are needed to improve the survival of patients with cancer. Vitamin D3, 1,25-dihydroxycholecalciferol D3, has been shown to induce apoptosis in the human breast cancer cell line, MCF-7. The authors have studied the effects of three concns. of vitamin D3 on the human breast cancer cell line, MDA-MB-435, the human prostate cancer cell line, LNCaP, and a human osteosarcoma cell line, U2OS. The authors report that vitamin D3 strikingly inhibits cell proliferation and induces apoptosis in all three cell lines.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:630002 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:287835
ORIGINAL REFERENCE NO.: 127:56053a,56056a

TITLE: 1α,25-Dihydroxyvitamin D (calcitriol) inhibits the invasiveness of human prostate cancer cells
AUTHOR(S): Schwartz, Gary G.; Wang, Ming-Hui; Zhang, Ming; Singh, Raj K.; Siegal, Gene P.
CORPORATE SOURCE: Sylvester Comprehensive Cancer Center, Dep. Epidemiol. Public Health, Univ. Miami, Miami, FL, 33101, USA
SOURCE: Cancer Epidemiology, Biomarkers & Prevention (1997), 6(9), 727-732
CODEN: CEBPE4; ISSN: 1055-9965
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1α,25-Dihydroxyvitamin D (1,25 Da; also known as calcitriol), the hormonal form of vitamin D, can inhibit the proliferation and promote the differentiation of human prostate adenocarcinoma cells. However, little is known about the effects of 1,25 Da on the invasive ability of prostate cancer cells. The authors used an in vitro bioassay of cell invasion (Amgel assay) to examine the effects of 1,25 Da and a "noncalcemic" vitamin D analog, 1,25-dihydroxy-16-ene-23-yne-cholecalciferol (16-23 Da3), on the invasiveness of three well-characterized human prostate carcinoma cell lines: DU 145, PC-3, and LNCaP. PC-3 and LNCaP cells were poorly invasive in Amgel and were hardly affected by treatment with 1,25 Da or 16-23 Da3 (<3%). Conversely, DU 145 cells were highly invasive in Amgel, and their invasion was markedly inhibited by 1,25 Da and 16-23 Da3 (maximally 66 and 59.4%, resp.). This effect was both dose-dependent (doses of 1 x 10-7-1 x 10-13 M) and time-dependent, with maximal inhibition at 1 x 10-7 M and 72 h. Significant inhibition of invasion was observed at physiol. levels of 1,25 Da. Neither proliferative indexes nor cell cycle kinetics were altered during the exptl. exposures. Treatment with 1,25 Da and 16-23 Da3 caused a selective decrease in the secreted levels of type IV collagenases (MMP-2 and MMP-9). These findings support the hypothesis that 1,25 Da reduces the risk of invasive prostate cancer and suggest a role for vitamin D compds. in the chemoprevention of invasive prostate cancer.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:560550 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:200563
ORIGINAL REFERENCE NO.: 127:38803a,38806a
TITLE: Three synthetic vitamin D analogs induce prostate-specific acid phosphatase and prostate-specific antigen while inhibiting the growth of human prostate cancer cells in a vitamin D receptor-dependent fashion
AUTHOR(S): Hedlund, Tammy E.; Moffatt, Kirsten A.; Uskokovic, Milan R.; Miller, Gary J.
CORPORATE SOURCE: Department of Pathology, University of Colorado Health Sciences Center, Denver, CO, 80262, USA
SOURCE: Clinical Cancer Research (1997), 3(8), 1331-1338
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous studies have indicated that the secosteroid hormone 1α,25-dihydroxyvitamin D3 protects against the development of clin. prostate cancer (PC). Whether this hormone also has therapeutic potential for patients with advanced PC has not yet been evaluated.

Several synthetic vitamin D analogs are now available that have reduced hypercalcemic effects and yet effectively induce differentiation in some cell types. For these reasons, these analogs may be safer and more effective for cancer therapy than the natural hormone. In the current study, 13 such analogs were screened for their abilities to inhibit the growth of PC cell lines. Three of the most consistently effective analogs (Ro 23-7553, Ro 24-5531, and Ro 25-6760) were then chosen for further anal. Growth studies using clones of the JCA-1 cell line that were transfected with the vitamin D receptor cDNA indicate that the antiproliferative effects of these analogs require vitamin D receptor expression. Furthermore, these three analogs induce the secretion of prostate-specific acid phosphatase and prostate-specific antigen (two markers of the differentiated prostatic phenotype) in the cell line LNCaP. These in vitro studies suggest that Ro 23-7553, Ro 24-5531, and Ro 25-6760 should be further evaluated as therapeutic agents for the treatment of PC.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:533277 CAPLUS <<LOGINID::20090601>>

DOCUMENT NUMBER: 127:242795

ORIGINAL REFERENCE NO.: 127:47211a,47214a

TITLE: Inhibition of proliferation of prostate cancer cells by a 19-nor-hexafluoride vitamin D3 analog involves the induction of p21waf1, p27kip1 and E-cadherin

AUTHOR(S): Campbell, M. J.; Elstner, E.; Holden, S.; Uskokovic, M.; Koeffler, H. P.

CORPORATE SOURCE: Div. Hematol./Oncol., Cedars-Sinai Med. Cent., UCLA Sch. Med., Los Angeles, CA, 90048, USA

SOURCE: Journal of Molecular Endocrinology (1997), 19(1), 15-27
CODEN: JMLEEI; ISSN: 0952-5041

PUBLISHER: Journal of Endocrinology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have synthesized and studied the ability of a series of seven novel 1α,25(OH)2vitamin D3 analogs to inhibit clonal growth of prostate cancer cells (LNCaP, PC-3 and DU-145). Addition of double and triple bonds to the C/D ring (C-16) and side chain (C-22 and C-23) as well as lengthening of the side chain were important for enhanced activity against LNCaP and PC-3. Reorientation of the side chain in the 20-epi configuration resulted in analogs that were extremely potent only against LNCaP (ED50 ≈5 + 10-11 M). Compds. with six fluorines on the end of the side chain were very active against both PC-3 and LNCaP (ED50 ≈2 + 10-8 M). DU-145 cells were relatively resistant to compds. with all of these modifications, but removal of C-19 (e.g. 1,25(OH)2-16-ene-23-yne-26,27-F6-19-nor-D3) resulted in an analog that was inhibitory against all three prostate cell lines. Further anal. showed that pulse exposure (3 days, 10-7 M) to this analog was enough to inhibit clonal growth of PC-3 cells by 50%. The same exposure also induced cell cycle arrest of all three cell lines, accompanied by upregulated protein expression of the cyclin-dependent kinase inhibitor (CDKI) known as p21waf1 in all three cell lines, and the CDKI known as p27kip1in LNCaP cells. Associated with upregulation of these CDKIs, partial differentiation occurred as measured by increased expression of both prostate-specific antigen by LNCaP cells and E-cadherin, a cell adhesion protein that may act as a putative tumor suppressor (LNCaP and PC-3 cells). In summary, this is the first report of a potent series of 19-nor-vitamin D3 analogs with the ability to inhibit proliferation of

LNCaP, PC-3 and DU-145 prostate cancer cell lines. These compds. may mediate their potent anti-proliferative activities through a cell cycle arrest pathway.

L19 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:520173 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:200524
ORIGINAL REFERENCE NO.: 127:38794h,38795a
TITLE: Vitamin D3 analogs and their 24-oxo metabolites equally inhibit clonal proliferation of a variety of cancer cells but have differing molecular effects
AUTHOR(S): Campbell, Moray J.; Reddy, G. Satyanarayana; Koeffler, H. Phillip
CORPORATE SOURCE: Division of Hematology/Oncology, Cedars-Sinai Medical Center/UCLA School of Medicine, Los Angeles, CA, 90048, USA
SOURCE: Journal of Cellular Biochemistry (1997), 66(3), 413-425
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The seco-steroid hormone, 1α,25-dihydroxyvitamin D3 (1α,25(OH)2D3) binds to a specific nuclear receptor that acts as a ligand-inducible transcription factor. The resulting genomic effects include partial arrest in G0/G1 of the cell cycle and induction of differentiation; these effects have been observed in various types of cancer. Recently, we produced enzymically the natural 24-oxo metabolites of 1α,25(OH)2D3 and two of its potent synthetic analogs (1α,25-(OH)2-16-ene-D3 and 1α,25-(OH)2-20-epi-D3) using a rat kidney perfusion system. We have found that the 24-oxo metabolites of both 1α,25(OH)2D3 and its analogs have either the same or greater antiproliferative activity against various cancer cells as their parental compds. Notably, two cell lines (DU-145 (prostate cancer) and MDA-MB-436 [breast cancer]) that were extremely resistant to the antiproliferative effects of vitamin D3 analogs displayed greater sensitivity towards the 24-oxo metabolite of the vitamin D3 analog. Similarly, the 24-oxo metabolites had the capacity to induce differentiation and apoptosis and to diminish the proportion of cells in S phase. Most interestingly, while the analog 1α,25(OH)2-20-epi-D3 induced expression of BRCA1 in MCF-7 breast cancer cells; its 24-oxo metabolite dramatically suppressed BRCA1 expression. Thus, we have shown for the first time that the various biol. activities produced by the hormone 1α,25(OH)2D3 and some its analogs may represent a combination of actions by the hormone 1α,25(OH)2D3 and its natural 24-oxo metabolites.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:470218 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:157122
ORIGINAL REFERENCE NO.: 127:30299a,30302a
TITLE: 1α,25-Dihydroxyvitamin D3 actions in LNCaP human prostate cancer cells are androgen-dependent
AUTHOR(S): Zhao, Xiao-Yan; Ly, Lan H.; Peehl, Donna M.; Feldman, David
CORPORATE SOURCE: Departments of Medicine and Urology, Stanford University School of Medicine, Stanford, CA, 94305, USA
SOURCE: Endocrinology (1997), 138(8), 3290-3298

CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors and others have recently shown that 1α,25-dihydroxyvitamin D3 [1,25-(OH)2D3] significantly inhibits cell proliferation and increases secretion of prostate-specific antigen (PSA) in LNCaP cells, an androgen-responsive human prostate cancer cell line. The present study was designed to investigate the possible interactions between 1,25-(OH)2D3 and androgens in the regulation of LNCaP cellular function. LNCaP cell growth was dose-dependently inhibited by 1,25-(OH)2D3 (60% inhibition at 10 nM) when cells were cultured in medium supplemented with FBS (FBS medium). 1,25-(OH)2D3-treated cells showed a 5-fold increase in PSA secretion, similar to the increase seen in dihydrotestosterone (DHT)-treated cells. In combination, 1,25-(OH)2D3 and DHT synergistically enhanced PSA secretion 22-fold. This synergistic effect was even greater when cells were cultured in medium supplemented with charcoal-stripped serum (CSS medium), where endogenous steroids are substantially depleted. Under these conditions, 1,25-(OH)2D3 and DHT together stimulated PSA secretion up to 50-fold over the untreated control. Radioligand binding assays and Western blot analyses showed that the androgen receptor (AR) content was increased significantly by 1,25-(OH)2D3 at 48 h. Furthermore, the steady-state mRNA level of AR was up-regulated approx. 2-fold by 1,25-(OH)2D3 at 24 h. When cells were grown in CSS medium, 1,25-(OH)2D3 alone no longer inhibited cell growth or induced PSA secretion. Titration expts. revealed that the addition of DHT at 1 nM to the medium restored the antiproliferative activity of 1,25-(OH)2D3. Conversely, an antiandrogen, Casodex, completely blocked 1,25-(OH)2D3 antiproliferative and PSA stimulation activities when cells were cultured in FBS medium. In conclusion, these results demonstrate that the antiproliferative and PSA induction activities of 1,25-(OH)2D3 in LNCaP cells are dependent upon androgen action and that AR up-regulation by 1,25-(OH)2D3 likely contributes to the synergistic actions of 1,25-(OH)2D3 and DHT in these cells.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:323038 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 127:13753
ORIGINAL REFERENCE NO.: 127:2703a,2706a
TITLE: Effects of potent vitamin D3 analogs on clonal proliferation of human prostate cancer cell lines
AUTHOR(S): De Vos, Sven; Holden, Stuart; Heber, David; Elstner, Elena; Binderup, Lise; Uskokovic, Milan; Rude, Bob; Chen, Dan Lin; Le, Jennifer; et al.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine, Cedars-Sinai Research Institute, UCLA School of Medicine, Los Angeles, CA, 90048, USA
SOURCE: Prostate (New York) (1997), 31(2), 77-83
CODEN: PRSTDS; ISSN: 0270-4137
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Management of prostate cancer that has spread outside of the prostate capsule is a difficult problem. Innovative, non-toxic approaches to the disease are required. New, relatively non-toxic vitamin D3 analogs have recently been synthesized. The authors report that several of these compds. have marked antiproliferative effects on

prostate cells. The clonal antiproliferative activity of five novel analogs of 1,25 dihydroxyvitamin D3 [1,25(OH)2D3, (compd C)] as well as 1,25(OH)2D3 itself was tested on three human prostate cancer cell lines (PC-3, LNCaP, and DU-145). The analogs were 20-epi-22oxa-24a,26a,27a-tri-homo-1α,25(OH)2D3 (code name: KH 1060); 24a26a27a-tri-homo-22,24-diene-1α,25(OH)2D3 (code name: EB 1089); 1,25(OH)2-16ene-D3 (code name: HM); 1,25(OH)2-16ene-23yne-D3 (code name: V); 1,25(OH)2-20-epi-D3 (code name: MC 1288). With the parent compound [1,25(OH)2D3], the ED that inhibited 50% clonogenic growth of PC-3 and LNCaP was 10-8M and 7+10-9 M, resp. For these prostate cancer cell lines, KH 1060 was the most potent analog by an order of 25- to 35-fold as compared to compd C. The second and third most potent analogs were HM and MC 1288. DU-145 was resistant to all the vitamin D3 analogs. The major side-effect of 1,25(OH)2D3 is the production of hypercalcemia. The relative inhibitory index (RII) was determined by comparing the antiproliferative activity of the analog to its ability to produce hypercalcemia in mice injected i.p. every other day. The KH 1060 had the best RTI: 50- to 70-fold greater than 1,25(OH)2D3 for PC-3 and LNCaP, resp. A trial of one or more of these innovative compds. should be considered for treatment of minimal residual disease of prostate cancer.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:17397 CAPLUS <<LOGINID::20090601>>

DOCUMENT NUMBER: 126:113616

ORIGINAL REFERENCE NO.: 126:21849a,21852a

TITLE: Vitamin D receptor content and transcriptional activity do not fully predict antiproliferative effects of vitamin D in human prostate cancer cell lines

AUTHOR(S): Zhuang, S-H.; Schwartz, G. G.; Cameron, D.; Burnstein, K. L.

CORPORATE SOURCE: Departments of Molecular and Cellular Pharmacology, University of Miami School of Medicine, Miami, FL, 33136, USA

SOURCE: Molecular and Cellular Endocrinology (1997), 126(1), 83-90
CODEN: MCEND6; ISSN: 0303-7207

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Prostate cancer cell lines exhibit variable growth suppression by the hormonal form of vitamin D3, 1,25-Dihydroxyvitamin D3 [1,25(OH)2D] (1,25 D3). To understand the mol. basis for this differential sensitivity to 1,25 D3, the authors compared growth response to 1,25 D3, vitamin D receptor (VDR) content and VDR transcriptional activity in four well-characterized human prostate cancer cell lines: LNCaP, DU145, PC-3 and ALVA-31. In PC-3 and DU145 cells, relative lack of growth inhibition by 1,25 D3 (<10% inhibition) correlates with very low levels of VDR (9-15 fmol/mg protein) compared to classical vitamin D3 target tissues (.apprx.75-200 fmol/mg protein). Transfection of DU145 and PC-3 cells with a VDR cDNA expression vector is sufficient to establish growth sensitivity to 1,25 D3, suggesting that low VDR levels are responsible for the failure of these cell lines to respond to 1,25 D3. LNCaP cells are highly sensitive to growth inhibition by 1,25 D3 (.apprx.55% inhibition) and contain .apprx.2-3-fold more VDR (25 fmol/mg) than the relatively 1,25 D3-insensitive PC-3 and DU145 cell lines. However, ALVA-31 cells display less than 20% growth inhibition to 1,25 D3 although they contain the highest levels of VDR (45 fmol/mg) of the four cell lines. Thus,

sensitivity to growth inhibition by 1,25 D3 does not correlate with VDR content in ALVA-31 and LNCaP cells. This lack of correlation between VDR d. and growth responses to 1,25 D3 led the authors to investigate VDR-mediated gene transcription in these cell lines. The authors employed two different naturally-occurring vitamin D response elements (VDREs) linked to a reporter gene. Reporter gene activation by 1,25 D3 correlated well with VDR content in all four cell lines. Therefore, compared to LNCaP cells, decreased sensitivity of ALVA-31 to growth inhibition by 1,25 D3 is not due to a decrease in the general transcriptional activity of VDR. The authors conclude that growth inhibition by 1,25 D3 in prostate cancer cells requires VDR but that this response is modulated by non-receptor factors that are cell line-specific.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:698727 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 125:316553
ORIGINAL REFERENCE NO.: 125:58943a,58946a
TITLE: The differentiating agent phenylacetate increases prostate-specific antigen production by prostate cancer cells
AUTHOR(S): Walls, Ronald; Thibault, Alain; Liu, Lei; Wood, Chris; Kozlowski, James M.; Figg, William D.; Sampson, Maureen L.; Elin, Ronald J.; Samid, Dvorit
CORPORATE SOURCE: Clinical Pathology Department, National Cancer Institute, Bethesda, MD, USA
SOURCE: Prostate (New York) (1996), 29(3), 177-182
CODEN: PRSTDS; ISSN: 0270-4137
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prostatic-specific antigen (PSA) is the tumor marker most widely relied upon for the monitoring of patients with prostate cancer. Recently, declines in the serum concns. of PSA have been advocated as a surrogate marker of tumor response in clin. trials of investigational antitumor agents. We examined the hypothesis that this postulate may not apply to the evaluation of drugs such as phenylacetate, a differentiating agent endowed with mechanisms of action different from those of classic cytotoxic chemotherapy. Using human prostatic carcinoma LNCaP cells as a model, we show that phenylacetate induces PSA production despite inhibition of tumor cell proliferation. Incubation of LNCaP cultures with cytostatic doses of phenylacetate (3-10 mM) resulted in a three- to fourfold increase in PSA secretion per cell. This appears to result from upregulation of PSA gene expression, as indicated by elevated PSA mRNA steady-state levels in treated cells. The increase in PSA production per cell was confirmed in rats bearing s.c. LNCaP tumor implants that were treated systemically with phenylacetate. Further comparative studies indicate that upregulation of PSA is common to various differentiation inducers, including all-trans-retinoic acid, 1,25-dihydroxyvitamin D3, and butyrate but is not induced by other antitumor agents of clin. interest such as suramin. We conclude that declines in PSA may be treatment specific and that the exclusive use of this criterion as a marker of disease response may mislead the proper evaluation of differentiating agents in prostate cancer patients.

L19 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:672248 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 125:318815
ORIGINAL REFERENCE NO.: 125:59527a
TITLE: Effects of 1,25 dihydroxyvitamin D3 and its analogs on

induction of apoptosis in breast cancer cells
AUTHOR(S): James, Sharon Y.; Mackay, Alan G.; Colston, Kay W.
CORPORATE SOURCE: Dep. Clinical Biochemistry, St. George's Hospital Med. Sch., London, SW17 0RE, UK
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1996), 58(4), 395-401
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vitamin D derivs. have been shown both to inhibit the proliferation of cultured breast cancer cells and to cause regression of exptl. mammary tumors in vivo. The authors have investigated the ability of several vitamin D analogs to promote the regression of exptl. rat mammary tumors. The authors' results revealed that one vitamin D compound in particular, EB1089 was highly effective at inhibiting tumor progression, without causing a significant rise in serum calcium concentration Tumor regression occurs when the rate of cell death is greater than the rate of cell proliferation. Apoptosis (programmed or active cell death) is an active, energy-dependent process in which a distinct series of biochem. and mol. events leads to the death of cells by specific signals. The authors have examined effects of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) and the synthetic vitamin D analog EB1089 on indexes of apoptosis in cultured human breast cancer cells. The effects of the vitamin D compds. on the expression of two oncoproteins which may regulate apoptosis, bcl-2 and p53 were examined by Western anal. In MCF-7 cells cultures treated for six days with 1,25(OH)2D3 or EB1089 (1 + 10-8 M), bcl-2 protein was reduced in comparison to control levels, whereas p53 protein was increased. In addition, the p21 protein, whose gene WAF-1 is induced by wild type p53, was also increased by both vitamin D compds. Using Northern anal., it was observed that 24-h treatment of MCF-7 cells with 1 + 10-8 M 1,25(OH)2D3 or EB1089 resulted in an induction of TRPM-2 (clusterin) mRNA, a gene associated with onset of apoptosis in the involuting prostate. Fragmentation of genomic DNA is a characteristic feature of apoptosis. With the terminal deoxynucleotidyl transferase (TdT) assay, 3'-OH DNA breaks indicative of DNA fragmentation were detected histochem. in MCF-7 cells treated with 1 + 10-8 M 1,25(OH)2D3 or EB1089 for four days prior to fixation and TdT reaction. Further evidence of apoptosis was obtained following six days treatment of MCF-7 cell cultures with 5 + 10-8 M, 1,25(OH)2D3 or EB1089, utilizing a cell death ELISA assay, which measures the presence of histone-associated oligonucleosome complexes generated from DNA fragmentation. Taken together the authors' findings indicate that vitamin D derivs. may play a role in regulating the expression of genes and protein products implicated in apoptosis.

L19 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:244194 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 124:306786
ORIGINAL REFERENCE NO.: 124:56539a,56542a
TITLE: Control of LNCaP proliferation and differentiation: Actions and interactions of androgens, 1α,25-dihydroxycholecalciferol, all-trans-retinoic acid, 9-cis-retinoic acid, and phenylacetate
AUTHOR(S): Esquenet, Murielle; Swinnen, Johannes V.; Heyns, Walter; Verhoeven, Guido
CORPORATE SOURCE: Department Developmental Biology, Catholic University Leuven, Louvain, B-3000, Belg.
SOURCE: Prostate (New York) (1996), 28(3), 182-94
CODEN: PRSTDS; ISSN: 0270-4137
PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is increasing evidence that growth and differentiation of prostatic carcinoma cells may be modulated not only by androgens and growth factors but also by vitamin D, retinoids, and phenylacetate (PA). The latter agonists may have a role in the prevention and therapy of prostate cancer but their exact therapeutic potential remains unclear. Since both retinoids and vitamin D act via nuclear receptors, the same way androgens do, we studied the interactions of these compds. with androgen-induced proliferation and differentiation using LNCaP cells as a model of androgen-responsive tumor cells. PA was included because of its suspected different mode of action. [3H]-thymidine incorporation was used as a measure of proliferative activity, secretion of prostate -specific antigen (PSA) as a measure of differentiated function. The present data show that 1α,25-dihydroxycholecalciferol (VD3), all-trans retinoic acid (atRA), 9-cis retinoic acid (9cRA), and PA stimulated LNCaP cell-differentiated function in the presence or absence of androgens. The effects on cell growth were more complicated. In the absence of androgens growth stimulatory effects were observed for the retinoids and under some conditions for VD3. These effects were limited, however, and tended to be more pronounced at low cell densities. In the presence of androgens nearly exclusively growth inhibitory effects were observed On a molar basis VD3 was the most effective antiproliferative agonist (ED50 = 10-9 M). It completely neutralized the stimulatory effects of androgens. Growth inhibition was not due to a decrease in the concentration of androgen receptor: whereas atRA, 9cRA, and PA did not alter androgen receptor levels, VD3 provoked a twofold increase. Neither in the presence nor in the absence of androgens did we observed any cooperativity in the growth stimulatory or inhibitory effects of VD3, atRA, or 9cRA. To test whether treatment with any of the studied agonists resulted in a phenotypic reversion and sustained growth arrest, LNCaP cells were pretreated with VD3, atRA, 9cRA, or PA for 6-12 days and reseeded at equal densities as untreated cells. In all cases tested [3H]-thymidine incorporation was restored within 6 days suggesting that none of these compds. caused irreversible growth inhibition.

L19 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:870552 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:276705
ORIGINAL REFERENCE NO.: 123:49283a,49286a
TITLE: Vitamin D receptor expression, 24-hydroxylase activity, and inhibition of growth by 1α,25-dihydroxyvitamin D3 in seven human prostatic carcinoma cell lines
AUTHOR(S): Miller, Gary J.; Stapleton, Gary E.; Hedlund, Tammy E.; Moffatt, Kirsten A.
CORPORATE SOURCE: Health Sciences Center, University Colorado, Denver, CO, 80262, USA
SOURCE: Clinical Cancer Research (1995), 1(9), 997-1003
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although prostatic cancer is often viewed as an androgen-dependent malignancy, a number of other hormones including 1α,25-dihydroxyvitamin D3 [1α,25(OH)2D3] are now recognized to modulate its growth and differentiated phenotype. Seven different continuous human prostatic carcinoma cell lines were examined for the presence of biol. active receptors for 1α,25(OH)2D3. All seven lines were found to contain mRNA for the vitamin D receptor using an RNase protection assay. Six of the seven cell lines were found to have high-affinity saturable binding

sites for 1α,25(OH)2D3. The seventh line was found to contain vitamin D receptors by sucrose gradient anal. All seven lines were found to express 24-hydroxylase activity by a HPLC assay that measures the conversion of 25-hydroxyvitamin D3 to 24,25-dihydroxyvitamin D3. 24-Hydroxylase activity was up-regulated in all seven cell lines by preincubation with 1α,25(OH)2D3. In the presence of fetal bovine serum, the growth of four of the seven cell lines was inhibited. In the majority of cell lines growth inhibition was related not only to the number of receptors per cell, but also in inverse proportion to the 24-hydroxylase activity of each cell line. The ubiquitous presence of vitamin D receptor and 24-hydroxylase activity in human prostatic carcinoma cells suggests new alternatives for the pharmacol. treatment of advanced prostatic cancer and implies that chemoprevention strategies could also make use of this endocrine axis.

L19 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:619536 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 123:1100
ORIGINAL REFERENCE NO.: 123:239a,242a
TITLE: Vitamin D and cancer
AUTHOR(S): Verstuyf, A.; Mathieu, Chantal; Verlinden, L.; Bouillon, R.
CORPORATE SOURCE: Louvain, Belg.
SOURCE: Revue Francaise d'Endocrinologie Clinique, Nutrition et Metabolisme (1994), 35(4-5), 437-44
CODEN: RECNAS; ISSN: 0048-8062
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review, with 19 refs., on the treatment of cancers (particularly leukemia and breast and prostate cancers) with 1α,25-dihydroxyvitamin D3 and analogs.

L19 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:326434 CAPLUS <<LOGINID::20090601>>
DOCUMENT NUMBER: 122:96002
ORIGINAL REFERENCE NO.: 122:17899a,17902a
TITLE: Actions of vitamin D3 analogs on human prostate cancer cell lines: comparison with 1,25-dihydroxyvitamin D3
AUTHOR(S): Skowronski, Roman J.; Peehl, Donna M.; Feldman, David
CORPORATE SOURCE: Dep. Med. and Urology (D.M.P.), Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: Endocrinology (1995), 136(1), 20-6
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Data from epidemiol. studies has suggested that vitamin D deficiency may promote prostate cancer, although the mechanism is not understood. The authors have previously demonstrated the presence of vitamin D receptors (VDR) in three human prostate carcinoma cell lines (LNCaP, PC-3, and DU-145) as well as in primary cultures of stromal and epithelial cells derived from normal and malignant prostate tissues. The authors have also shown that 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] can elicit an antiproliferative action in these cells. In the present study the authors compared the biol. actions of 1,25-(OH)2D3 to those of a series of natural vitamin D3 metabolites and several synthetic analogs of vitamin D3 known to exhibit less hypercalcemic activity in vivo. In ligand binding competition expts., the authors demonstrated the following order of potency in displacing [3H]1,25-(OH)2D3 from VDR: EB-1089 > 1,25-(OH)2D3 > MC-903 > 1,24,25(OH)3D3 >

22-oxacalcitriol (OCT) > 1α,25-dihydroxy-16-ene-cholecalciferol (Ro 24-2637) > 25-hydroxyvitamin D3, with EB-1089 being .apprx.2-fold more potent than the native hormone. No competitive activity was found for 25-hydroxy-16,23-diene-cholecalciferol. When compared for ability to inhibit proliferation of LNCaP cells, MC-903, EB-1089, OCT, and Ro 24-2637 exhibited 4-, 3-, 3-, and 2-fold greater inhibitory activity than 1,25-(OH)2D3. Interestingly, although OCT and Ro 24-2637 exhibit, resp., 10 and 14 times lower affinity for VDR than 1,25-(OH)2D3, both compds. inhibited the proliferation of LNCaP cells with a potency greater than that of the native hormone. The relative potency of vitamin D3 metabolites and analogs to inhibit cell proliferation correlated well with the ability of these compds. to stimulate prostate-specific antigen secretion by LNCaP cells as well as with their potency to induce the 25-hydroxyvitamin D3-24-hydroxylase mRNA transcript in PC-3 cells. In conclusion, these results demonstrate that synthetic analogs of vitamin D3, known to exhibit reduced calcemic activity, can elicit antiproliferative effects and other biol. actions in LNCaP and PC-3 cell lines. It is noteworthy that although binding to VDR is critical for 1,25-(OH)2D3 action, the analog data indicate that addnl. factors significantly contribute to the magnitude of the biol. response. Finally, the strong antiproliferative effects of several synthetic analogs known to exhibit less calcemic activity than 1,25-(OH)2D3 suggest that these compds. potentially may be useful as an addnl. therapeutic option for the treatment of prostate cancer.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	53.46	204.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.48	-36.08

STN INTERNATIONAL LOGOFF AT 10:48:52 ON 01 JUN 2009